

CLAIMS

What is claimed is:

1. An adapter-directed display system for displaying an exogenous polypeptide on the outer surface of a genetic package, comprising:

- (a) an expression vector comprising a coding sequence that encodes the exogenous polypeptide fused in-frame to a first adapter sequence, wherein the vector is devoid of outer-surface sequences encoding any functional outer-surface proteins of the genetic package;
- (b) a helper vector comprising outer-surface sequences encoding outer-surface proteins necessary for packaging the genetic package, wherein at least one of the outer-surface protein is fused in-frame to a second adapter, said first and second adapter acting, when the polypeptide is produced in a suitable host cell, to cause the display of the polypeptide via pairwise interaction between the first and second adapters.

2. The adapter-directed display system of claim 1, wherein the system is a phage display system.

3. The adapter-directed display system of claim 1, wherein the system is a bacterial display system.

4. The adapter-directed display system of claim 1, wherein the genetic package is selected from the group consisting of viruses, cells, and spores.

5. The adapter-directed display system of claim 2, wherein the outer-surface sequences encode functional coat proteins of a phage.

6. The adapter-directed display system of claim 2, wherein the phage is a filamentous phage.

7. The adapter-directed display system of claim 2, wherein in the outer-surface sequences are selected from the group consisting of gene III, gene VI, gene VII, gene VIII, and gene IX of a filamentous phage.

8. The adapter-directed display system of claim 3, wherein the outer-surface sequences encode bacterial outer-surface proteins.

9. The adapter-directed display system of claim 3, wherein the bacterial outer-surface proteins are selected from the group consisting of Lpp-OmpA, TraT, Pal, Oprl, Inp and AIDA-I.

10. The adapter-directed display system of claim 1, wherein the first and second adapters are homodimerization sequences.

11. The adapter-directed display system of claim 1, wherein the homodimerization sequences consist of a pair of cysteine residues.

12. The adapter-directed display system of claim 1, wherein the first and second adapters are heterodimerization sequences.

13. The adapter-directed display system of claim 1, wherein the first and second adapters form a coiled-coil dimer.

14. The adapter-directed display system of claim 13, wherein the first and second adapters are leucine zippers.

15. The adapter-directed display system of claim 13, wherein the first and second adapters comprise heterodimeric receptor sequences that mediate heterodimerization of the receptors.

16. The adapter-directed display system of claim 13, wherein the first and second adapters comprise heterodimerization sequences of GABA<sub>B</sub> receptor 1 and GABA<sub>B</sub> receptor 2, respectively.

17. The adapter-directed display system of claim 13, wherein the first and second adapters comprise heterodimerization sequences of GABA<sub>B</sub> receptor 2 and GABA<sub>B</sub> receptor 1, respectively.

18. The adapter-directed display system of claim 1, wherein the helper vector further comprises at least one additional copy of outer-surface sequence that competes for packaging with the fusion outer-surface sequence in (b).

19. The adapter-directed display system of claim 2, wherein the expression vector is selected from the group consisting of pABMX14 shown in Figure 9A, pABMX15 shown in Figure 15A.

20. The adapter-directed display system of claim 2, wherein the phage helper vector is selected from the group consisting of GM-UltraHelper phage vector shown in Figure 5A, CM-UltraHelper phage vector shown in Figure 13A, and GMCT-UltraHelper phage vector shown in Figure 19A.

21. A helper vector for displaying a polypeptide on the outer surface of a genetic package comprising: outer-surface sequences necessary for packaging the genetic package, wherein at least one of the surface presenting sequences is fused in-frame to an adapter, said adapter acting, when the polypeptide is produced in a suitable host cell, to cause the display of the polypeptide.

22. The helper vector of claim 21, wherein the vector is a phage helper vector.

23. The helper vector of claim 21, wherein the vector is a bacterial helper vector.

24. The helper vector of claim 21, wherein the genetic package is selected from the group consisting of viruses, cells, and spores.

25. The helper vector of claim 22, wherein the outer-surface sequences encode functional coat proteins of a phage.

26. The helper vector of claim 22, wherein the phage is filamentous phage.

27. The helper vector of claim 22, wherein in the outer-surface sequences are selected from the group consisting of gene III, gene VI, gene VII, gene VIII, and gene IX of a filamentous phage.

28. The helper vector of claim 23, wherein the outer-surface sequences encode bacterial outer-surface proteins.

29. The helper vector of claim 23, wherein the bacterial outer-surface proteins are selected from the group consisting of Lpp-OmpA, TraT, Pal, Oprl, Inp and AIDA-I.

30. The helper vector of claim 21, wherein the adapter causes the display of the polypeptide via pairwise interaction with a second adapter, which is fused in-frame with the polypeptide.

31. The helper vector of claim 21, wherein the adapter causes the display of the polypeptide in the absence of expression of an outer-surface protein via a phagemid vector or a plasmid.

32. The helper vector of claim 21, wherein the two adapters are heterodimerization sequences.

33. The helper vector of claim 21, wherein the two adapters are homodimerization sequences.

34. The helper vector of claim 21, wherein the two adapters are homodimerization sequences.

35. The helper vector of claim 34, wherein the homodimerization sequences consist of a pair of cysteine residues.

36. The helper vector of claim 32, wherein the two adapters form a coiled-coil dimer.

37. The helper vector of claim 36, wherein the two adapters are leucine zippers.

38. The helper vector of claim 36, wherein the two adapters comprise heterodimeric receptor sequences that mediate heterodimerization of the receptors.

39. The helper vector of claim 36, wherein the two adapters comprise heterodimerization sequences of GABA<sub>B</sub> receptor 1 and GABA<sub>B</sub> receptor 2, respectively.

40. The helper vector of claim 36, wherein the two adapters comprise heterodimerization sequences of GABA<sub>B</sub> receptor 2 and GABA<sub>B</sub> receptor 1, respectively.

~~41.~~ An expression vector for producing a polypeptide within or on the outer surface of a genetic package, comprising: a coding sequence encoding the polypeptide fused in-frame to a first adapter, wherein the vector is devoid of outer-surface sequences encoding any functional outer-surface proteins of the genetic package, and expression of the polypeptide on the outer surface of the genetic package is mediated via non-covalent pairwise interaction between the first adapter and a second adapter, wherein the second adapter is fused to an outer-surface protein.

42. The expression vector of claim 41, wherein the vector is a phagemid vector.

43. The expression vector of claim 41, wherein the vector is a bacterial expression vector.

44. The expression vector of claim 41, wherein the genetic package is selected from the group consisting of viruses, cells, and spores.

45. The expression vector of claim 41, wherein the outer-surface sequences are phage coat-encoding gene sequences.

46. The expression vector of claim 41, wherein the outer-surface sequences encode bacterial outer-surface proteins.

47. The expression vector of claim 41, wherein the first and second adapters are homodimerization sequences.

48. The expression vector of claim 41, wherein the first and second adapters are heterodimerization sequences.

49. The expression vector of claim 41, wherein the first and second adapters form a coiled-coil dimer.

50. The expression vector of claim 49, wherein the first and second adapters are leucine zippers.

51. The expression vector of claim 41, wherein the first and second adapters comprise heterodimeric receptor sequences that mediate heterodimerization of the receptors.

52. The expression vector of claim 51, wherein the first and second adapters comprise heterodimerization sequences of GABA<sub>B</sub> receptor 1 and GABA<sub>B</sub> receptor 2, respectively.

53. The expression vector of claim 51, wherein the first and second adapters comprise heterodimerization sequences of GABA<sub>B</sub> receptor 2 and GABA<sub>B</sub> receptor 1, respectively.

54. A kit comprising the adapter-directed display system of claim 1 in suitable packaging.

55. A kit comprising the helper vector of claim 21 in suitable packaging.

56. A kit comprising the expression vector of claim 41 in suitable packaging.

57. A host cell comprising the adapter-directed display system of claim 1.

58. A host cell comprising the helper vector of claim 21.

59. A host cell comprising the expression vector of claim 41.

60. A method for displaying a polypeptide on the outer surface of a genetic package comprising causing the adapter-directed display system of claim 1 to be transcribed and translated in a suitable host cell.

61. A polypeptide displayed on the outer surface of a genetic package according to method of claim 60.

62. A genetic package displaying on its outer surface a fusion polypeptide, said fusion polypeptide comprising a polypeptide sequence to be displayed, fused in-frame with a first adapter, said first adapter acting, when the fusion polypeptide is produced in a suitable host cell, to cause the display of the fusion polypeptide via non-covalent pairwise interaction between the first adapter and a second adapter that is linked to an outer-surface protein.

63. The genetic package of claim 62, wherein the genetic package is selected from the group consisting of viruses, cells, and spores.

64. A selectable library comprising a plurality of genetic packages at least one being the genetic package of claim 63.

65. A selectable library comprising a plurality of genetic packages, at least one member of the plurality displaying a polypeptide on its outer surface according to the method of claim 60.

66. A method of detecting the presence of a specific interaction between a test agent and an exogenous polypeptide that is displayed on a genetic package, the method comprising:

- (a) providing a genetic package displaying the exogenous polypeptide that is prepared according to the method of claim 60;
- (b) contacting the genetic package with the test agent under conditions suitable to produce a stable polypeptide-agent complex; and
- (c) detecting the formation of the stable polypeptide-agent complex on the genetic package, thereby detecting the presence of a specific interaction.

67. The method of claim 66, wherein the exogenous polypeptide is selected from the group consisting of antigen-binding unit, cell surface receptor, receptor ligand, cytosolic protein, secreted protein, and nuclear protein.

68. The method of claim 66, wherein the exogenous polypeptide is an antigen-binding unit.

69. The method of claim 66, wherein the test agent is selected from the group consisting of protein, polysaccharides, lipid, and combinations thereof.

70. The method of claim 66, wherein the test agent is an antigen.

71. The method of claim 66, wherein the test agent is a ligand.

72. A method of obtaining a polypeptide with desired property, comprising:

(a) providing a selectable library of claim 65; and

(b) screening the selectable library to obtain at least one genetic package displaying a polypeptide with the desired property.

73. The method of claim 72, wherein the desired property is binding specificity to an agent of interest.

74. The method of claim 72, wherein the screening the selectable library further comprises isolating the genetic package that displays a polypeptide having the desired property.

75. The method of claim 72, wherein isolating the genetic package further comprises obtaining a nucleotide sequence from the genetic package that encodes the polypeptide with the desired property.

76. The method of claim 72, wherein the polypeptide with the desired property is selected from the group consisting of antigen-binding unit, cell surface receptor, receptor ligand, cytosolic protein, secreted protein, nuclear protein, and functional motif thereof.

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